SHORT PAPER

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(*E*)-Selective synthesis of γ-substituted-β-(ethoxycarbonyl)allylsilanes utilising ethyl 2-diphenylphosphono-3-(trimethylsilyl)propionate. Improved synthesis of 11 membered carbocycle by a homo-Cope reaction†

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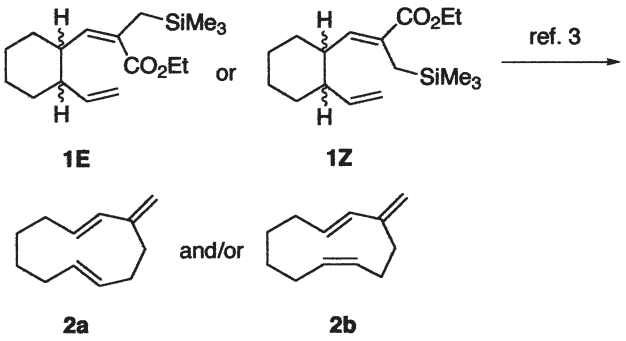
(***E***)-γ-Substituted-β-(ethoxycarbonyl)allylsilanes were selectively synthesised by Horner-Wadsworth-Emmons reaction utilising ethyl 2-diphenylphosphono-3-(trimethylsilyl)propionate.

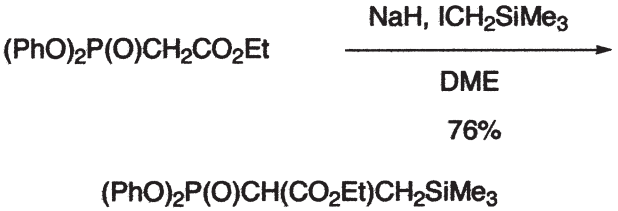
Keywords: Horner–Wadsworth–Emmons reaction, β-(ethoxycarbonyl)allylsilane, homo-Cope reaction

β-(Ethoxycarbonyl)allylsilane is a versatile three-carbon unit, which has been used in the synthesis of five-membered ring structure.[1, 2] There is often a different reactivity between (*E*)- and (*Z*)-isomers; the former is sometimes more useful in comparison with the latter. For example, we have recently reported a homo-Cope type of five-carbon ring expansion reaction utilising β-(hydroxymethyl)allylsilane, in which (*E*)-derivative **1E** afforded the desired product **2a**,**b** in high yield, whereas (*Z*)-derivative **1Z** gave a poor yield (Scheme 1).[3] Related results were obtained in the synthesis of guaianolide analogues. The intramolecular cyclisation of (*E*)-β-(ethoxycarbonyl)allylsilane with an acid chrolide afforded the product in much better yield than the (*Z*)-isomer.[1e]



Scheme 1

Though some methods for the synthesis of γ-substituted-β-(ethoxycarbonyl)allylsilanes from aldehydes and silylated reagents have been reported, most of them are (*Z*)-selective. For examples, Miginiac *et al.* obtained[4] (*Z*)-β-(ethoxycarbonyl)allylsilanes by the Lewis acid-promoted coupling of aldehydes and 1-ethoxy-3-(trimethylsilyl)propyne. Nishitani *et al.* reported[5] a (*Z*)-selective synthesis of this unit by β-elimination of 3-mesyloxy-2-(trimethylsilylmethyl)alkanoate. The Horner–Wadsworth–Emmons (HWE) reaction using ethyl 2-diethylphosphono-3-(trimethylsilyl)propionate as the phosphonate reagent, developed by Hoffmann *et al.*[6] is one of the most useful methods, by which the (*Z*)-isomer is normally obtained preferentially.[2b-e] On the other hand, Ando reported the (*Z*)-selective HWE reaction using ethyl (diaryl-phosphono)acetates in which a variety of aldehydes were converted to (*Z*)-α,β-unsaturated esters with high selectivity.[7] However, the phosphonate bearing hetero atom substituent has not been examined. Here we report the application of this Ando-HWE reaction in the (*E*)-selective synthesis of β-(ethoxycarbonyl)allylsilanes.



3

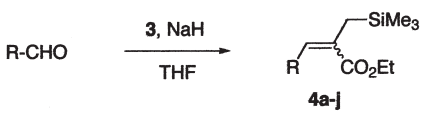
Scheme 2

The phosphonate reagent using in this study, ethyl 2-diphenylphosphono-3-(trimethylsilyl)propionate **3**, was prepared by the alkylation of ethyl (diphenylphosphono)acetate with (iodomethyl)trimethylsilane in a 76% yield (Scheme 2).

The results of the Ando-HWE reaction of the phosphonate **3** with several aldehydes are shown in Table 1. The reaction proceeded smoothly in all cases, providing γ-substituted-β-(ethoxycarbonyl)allylsilanes in high yields. The *E*/*Z* selectivities were excellent, leading to more than 90% of the (*E*)-isomers except for **4a**,**4d** and **4j**. The *E*/*Z* ratio was determined from the integral values of each olefinic protons in the ^{1}H NMR spectra[1b] (*e.g.* **4a**: δ 5.66, *Z*-**4a**: δ 6.60).

We then tried to apply this method to the synthesis of *trans*-**1E** , which is the intermediate for a five-carbon ring expansion

Table 1



4a-j

R	Product	Yield/%	*E*/*Z* ratio
n-C_7H_{15}	**4a**	97	80:20
n-BuCHEt	**4b**	91	98:2
trans-*n*-PrCH=CH	**4c**	99	93:7
Me_2C=CH	**4d**	86	78:22
trans-MeCH=Cme	**4e**	82	94:6
cyclohexyl	**4f**	86	98:2
1-cyclohexyl	**4g**	95	97:3
phyenyl	**4h**	94	98:2
RCHO=perillaldehyde	**4i**	91	96:4
PCHO=cinnamylaldehyde	**4j**	99	88:12

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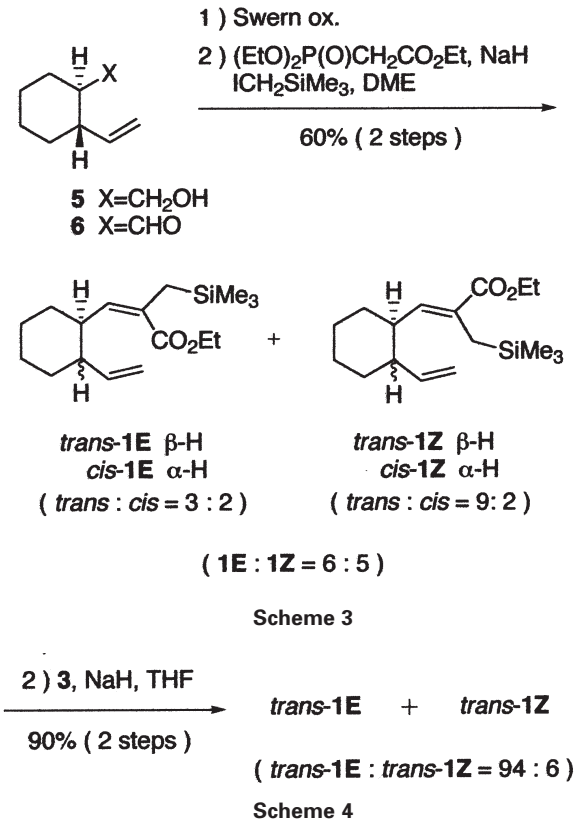
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

reaction.[3] In our previous work, the HWE reaction of the aldehyde **6**, obtained by Swern oxidation of **5**, afforded a mixture of (*E*)- and (*Z*)-β-(ethoxycarbonyl)allylsilanes in low selectivity (**1E** : **1Z** = 6 : 5). An isomerization at the α-carbon of the aldehyde also occurred giving the *cis*-isomer with respect to the cyclohexane ring *cis*-**1E**,**Z** (Scheme 3). When **6** was treated with an anion of the phosphonate **3**, the desired compound *trans*-**1E** was obtained in high yield (*trans*-**1E** : *trans*-**1Z** = 94 : 6). Moreover, isomerisation at the α-carbon of the aldehyde did not occur (Scheme 4). Under a weak-base condition, DBU/NaI, *trans*-**1E** was obtained in high selectivity (*trans*-**1E** : *trans*-**1Z** = 95 : 5). However the yield (78%) was lower than the case when NaH was used as the base. Since *trans*-**1Z** is useless in the five-carbon ring expansion reaction, the overall efficiency of the synthesis of eleven menbered carbocycles **2a**,**b** has been increased over our previous report.



Scheme 3

Scheme 4

In conclusion, we have established the (*E*)-selective synthesis of γ-substituted-β-(ethoxycarbonyl)allylsilanes utilising ethyl 2-diphenylphosphono-3-(trimethylsilyl)propionate as the phosphonate. Since a (*Z*)-selective synthesis has already been established,[4-6] it is possible to synthesise both the (*E*)- and (*Z*)-isomer selectively.

Experimental

All reactions were carried out under an Ar atmosphere. CH_2Cl_2 was distilled from CaH_2, 1,2-dimethoxyethane (DME) and tetrahydrofuran (THF) were distilled from $LiAlH_4$ just before use. Column chromatography was performed on silica gel (Wakogel C-200) with solvents shown in parenthesis. IR spectra were determined on a JASCO FT/IR-230 spectrometer. Both ^1H and ^{13}C NMR spectra were recorded on a JEOL GSX-400 (400 MHz for ^1H; 100 MHz for ^{13}C) spectrometer with $CDCl_3$ as the solvent. Chemical shifts are reported on the δ scale (ppm) with chloroform ($CHCl_3$ = 7.26 for ^1H; $CDCl_3$ = 77.00 for ^{13}C) as an internal standard. Both low-resolution mass spectra (MS) and high-resolution mass spectra (HRMS) were measured on a Shimadzu GCMS-QP5050, or a Jeol JMS-HX110 mass spectrometer with the EI method.

Ethyl 2-diphenylphosphono-3-(trimethylsilyl)propionate **(3):** a solution of ethyl 2-(diphenylphosphono)acetate (5.546 g, 17.32 mmol) in DME (15 ml), was added dropwise at 0°C to a stirred suspension of NaH (719.5 mg, 16.49 mmol) in DME (70 ml) and the stirring was continued for 30 min. After the solution had been allowed to warm to room temperature, (iodomethyl)trimethylsilane (3.00 ml, 20.04 mmol) was added dropwise, and the mixture was refluxed for 18 h. This was cooled to room temperature, quenched with saturated NH_4Cl aq (60 ml), and extracted with AcOEt (60 ml×3). The combined extracts were washed with water (50 ml×1) followed by brine, and dried ($MgSO_4$). Removal of the solvent left a residue which was chromatographed on silica gel (hexane : AcOEt = 9 : 1) to give **3** (5.316 g, 76%) as a colourless oil: IR (neat) 1737 cm^{-1}; ^1H NMR δ 0.04 (9H, s), 1.25 (1H, ddd, *J* = 2.4, 14.7, 17.1Hz), 1.28 (3H, t, *J* = 7.1Hz), 1.49 (1H, ddd, *J* = 8.1, 12.8, 14.7Hz), 3.29 (1H, ddd, *J* = 2.4, 12.8, 22.5Hz), 4.22 (2H, q, *J* = 7.1Hz), 7.14–7.21 (6H, m), and 7.28–7.34 (4H, m); ^{13}C NMR δ –1.73 (3C), 13.08 (d), 14.00, 41.36 (d), 61.74, 120.46 (2C, d), 120.54 (2C, d), 129.65 (4C), 150.32 (2C, d), 150.41 (2C, d), and 168.89 (d); MS *m/z* 391 (M^+-Me); Anal. Found: C, 59.04; H, 6.42%. Calcd for $C_{20}H_{27}O_5PSi$: C, 59.10; H, 6.70%.

General procedure for the synthesis of β-*(ethoxycarbonyl)allylsilanes* **(4a–j)**: was added dropwise at 0°C a solution of ethyl 2-diphenylphosphono-3-(trimethylsilyl)propionate **3** (0.42 mmol) in THF (1 ml), to a stirred suspension of NaH (0.48 mmol) in THF (1 ml) and the stirring was continued at 0°C for 30 min. The solution was cooled to –60°C, and a solution of aldehyde (0.3 mmol) in THF (1 ml) was added dropwise. After stirring for 30 min at –60°C, the reaction mixture was allowed to warm slowly to room temperature over 14h. The reaction was quenched by addition of saturated NH_4Cl aq (10 ml), and the mixture was extracted with AcOEt (10 ml × 3). The combined extracts were washed with water (20 ml × 2) followed by brine, dried ($MgSO_4$), and concentrated. The product was isolated by column chromatography (hexane : Et_2O = 99 : 1).

Ethyl (E)-2-(trimethylsilylmethyl)dec-2-enoate **(4a)**: An oil; IR (neat) 1635 and 1714 cm^{-1}; ^1H NMR δ –0.02 (9H, s), 0.88 (3H, t, *J* = 7.1Hz), 1.21–1.43 (10H, m), 1.30 (3H, t, *J* = 7.0Hz), 1.72 (2H, AB), 2.39 (2H, q, *J* = 7.6Hz), 4.17 (2H, q, *J* = 7.0Hz), and 5.66 (1H, t, *J* = 7.6Hz); ^{13}C NMR δ –1.67 (3C), 14.09, 14.27 22.64, 24.03, 29.16, 29.31, 29.64, 29.81, 31.84, 59.99, 129.10, 139.24, and 168.53; MS *m/z* 284 (M^+); HRMS [Found: *m/z* 284.2165 (M^+). Calcd for $C_{16}H_{32}O_2Si$: *M*, 284.2153].

Ethyl (E)-4-ethyl-2-(trimethylsilylmethyl)oct-2-enoate **(4b)**: An oil; IR (neat) 1635 and 1717 cm^{-1}; ^1H NMR δ -0.01 (9H, s), 0.84 (3H, t, *J* = 7.3Hz), 0.86 (3H, t, *J* = 6.8Hz), 1.11–1.35 (6H, m), 1.29 (3H, t, *J* = 7.2Hz), 1.34–1.48 (2H, m), 1.74 (2H, s), 2.77–2.88 (1H, m), 4.16 (2H, q, *J* = 7.2Hz), and 5.30 (1H, d, *J* = 10.5Hz); ^{13}C NMR δ –1.62 (3C), 11.79, 14.08, 14.25, 22.84, 24.35, 28.56, 29.60, 35.21, 40.37, 59.95, 129.35, 143.34, and 168.86; MS *m/z* 284 (M^+); HRMS [Found: *m/z* 284.2191 (M^+). Calcd for $C_{16}H_{32}O_2Si$: *M*, 284.2153].

Ethyl (2E,4E)-2-(trimethylsilylmethyl)oct-2,4-dienoate **(4c)**: An oil; IR (neat) 1593, 1635, and 1706 cm^{-1}; ^1H NMR δ 0.00 (9H, s), 0.91 (3H, t, *J* = 7.3Hz), 1.32 (3H, t, *J* = 7.1Hz), 1.44 (2H, six, *J* = 7.3Hz), 1.79 (2H, s), 2.12 (2H, ddt, *J* = 1.4, 7.6, 7.3Hz), 4.20 (2H, q, *J* = 7.1Hz), 5.81 (1H, dt, *J* = 15.2, 7.6Hz), 6.19 (1H, d, *J* = 11.5Hz), and 7.03 (1H, ddt, *J* = 11.5, 15.2, 1.4Hz); ^{13}C NMR δ –1.57 (3C), 13.75, 14.27, 22.26, 24.37, 34.98, 60.14, 126.71, 127.90, 137.58, 139.74, and 167.91; MS *m/z* 254 (M^+); HRMS [Found: *m/z* 254.1722 (M^+). Calcd for $C_{14}H_{26}O_2Si$: *M*, 254.1683].

Ethyl (E)-5-methyl-2-(trimethylsilylmethyl)hex-2,4-dienoate **(4d)**: An oil; IR (neat) 1586, 1632, and 1705 cm^{-1}; ^1H NMR δ 0.00 (9H, s), 1.31 (3H, t, *J* = 7.0Hz), 1.79 (3H, br s), 1.82 (2H, s), 1.85 (3H, br s), 4.20 (2H, q, *J* = 7.0Hz), 6.44 (1H, d, *J* = 11.6Hz), and 6.80 (1H, d quint, *J* = 11.6, 1.6Hz); ^{13}C NMR δ –1.64 (3C), 14.30, 18.04, 24.64, 26.75, 60.10, 122.54, 126.10, 133.02, 140.15, and 168.23; MS *m/z* 240 (M^+); HRMS [Found: *m/z* 240.1561 (M^+). Calcd for $C_{13}H_{24}O_2Si$: *M*, 240.1526].

Ethyl (E)-3-cyclohexyl-2-(trimethylsilylmethyl)prop-2-enoate **(4f)**: An oil; IR (neat) 1630 and 1713 cm^{-1}; ^1H NMR δ –0.03 (9H, s), 0.97–1.36 (5H, m), 1.30 (3H, t, *J* = 7.1Hz), 1.60-1.74 (5H, m), 1.80 (2H, s), 2.81 (1H, dtt, *J* = 9.7, 3.4, 11.0Hz), 4.17 (2H, q, *J* = 7.1Hz), and 5.46 (1H, d, *J* = 9.7Hz); ^{13}C NMR δ –1.76 (3C), 14.21, 23.91, 25.76 (2C), 26.02, 33.16 (2C), 38.27, 59.97, 127.24, 144.56, and 168.52; MS *m/z* 268 (M^+); HRMS [Found: *m/z* 268.1868 (M^+). Calcd for $C_{15}H_{28}O_2Si$: *M*, 268.1839].

Ethyl (E)-3-phenyl-2-(trimethylsilylmethyl)prop-2-enoate **(4h)**: An oil; IR (neat) 1627 and 1717 cm^{-1}; ^1H NMR δ –0.02 (9H, s), 1.09 (3H, t, *J* = 7.5Hz), 1.91 (2H, AB), 4.08 (2H, q, *J* = 7.5Hz), 6.49 (1H, s), and 7.17-7.30 (5H, m); ^{13}C NMR δ –1.57 (3C), 13.69, 25.82, 60.52, 127.01, 127.92 (2C), 127.94 (2C), 130.95, 132.99, 136.99, and

170.15; MS *m/z* 262 (M^+); HRMS [Found: *m/z* 262.1389 (M^+). Calcd for $C_{15}H_{22}O_2Si$: *M*, 262.1370].

Ethyl 2-(trimethylsilylmethyl)cinnamate **(4j)**: An oil; IR (neat) 1588, 1615, and 1702 cm^{-1}; ^1H NMR δ 0.03 (9H, s), 1.36 (3H, t, *J* = 7.1Hz), 1.89 (2H, s), 4.26 (2H, q, *J* =7.1Hz), 6.39 (1H, dd, *J* = 0.8, 11.4Hz), 6.61 (1H, d, *J* = 15.8Hz), 7.20–7.37 (3H, m), 7.45 (2H, d, *J* = 6.9Hz), and 7.86 (1H, dd, *J* = 11.4, 15.8Hz); ^{13}C NMR δ –1.53 (3C), 14.33, 25.02, 60.34, 126.35, 126.83 (2C), 127.93, 128.59 (2C), 129.60, 136.10, 137.10, 137.21, and 167.69; MS *m/z* 288 (M^+); HRMS [Found: *m/z* 288.1542 (M^+). Calcd for $C_{17}H_{24}O_2Si$: *M*, 288.1526].

Spectroscope data for **4e**, **4g**, and **4i** are already recorded.[1b]

Ethyl (E)-2-trimethylsilylmethyl-3-(trans-2-vinylcyclohex-1-yl) prop-2-enoate (trans-1E):

Swern oxidation: DMSO (0.28 ml, 3.95 mmol) was added dropwise to a stirred solution of $(COCl)_2$ (0.25 ml, 2.87 mmol) in dry CH_2Cl_2 (7 ml) at –60°C. After stirring for 5 min, a solution of *trans*-2-vinylcyclo-hexanemethanol **5** (133.7 mg, 0.95 mmol) in dry CH_2Cl_2 (3 ml) was added dropwise to this solution. The reaction mixture was stirred for 1h at the same temperature followed by the addition of Et_3N (0.80 ml, 5.69 mmol). After this mixture was allowed to warm to room temperature, the stirring was continued for 50 min. Water (20 ml) was added, and the mixture was extracted with CH_2Cl_2 (10 ml × 3). The combined extracts were washed with water (20 ml × 2) followed by brine, dried (Na_2SO_4), and concentrated to give an oily residue (223.6 mg).

Ando-HWE reaction: To a stirred solution of the phosphonate reagent, generated from NaH (66.8 mg, 1.53 mmol; 55% in mineral oil which was not removed) and **3** (699.8 mg, 1.72 mmol) in THF (totally 5 ml) by the procedure described for **4a–j** was added dropwise a solution of the above residue (223.6 mg) in THF (3 ml) at –60°C. After stirring for 30 min, the reaction mixture was allowed to warm slowly to room temperature over 18h, followed by the same work up as described above. The product was isolated by silica gel (10 g) column chromatography (hexane : Et_2O = 99.5 : 0.5) to give the mixture of *trans*-**1E** and *trans*-**1Z** (254.0 mg, 90%) in 95 : 5 ratio. *trans*-**1E**: An oil; IR (neat) 1639 and 1712 cm^{-1}; ^1H NMR δ -0.03 (9H, s), 1.01–1.11 (1H, m), 1.12–1.30 (3H, m), 1.30 (3H, t, *J* = 6.8Hz), 1.70 (2H, AB), 1.67–1.78 (5H, m), 2.78 (1H, ddt, *J* = 3.6, 11.6, 10.0Hz), 4.16 (2H, q, *J* = 6.8Hz), 4.85 (1H, dd, *J* = 1.6, 10.0Hz), 4.92 (1H, dd, *J* = 1.6, 17.2 Hz), 5.41 (1H, d, *J* = 10.0 Hz), and 5.64 (1H, ddd, *J* = 7.6, 10.0, 17.2 Hz); ^{13}C NMR δ –1.61 (3C), 14.23, 23.97, 25.64, 25.83, 32.60, 32.90, 42.68, 48.16, 59.94, 113.20, 127.98, 143.46, 144.09, and 168.46; MS *m/z* 294 (M^+); HRMS [Found: *m/z* 294.1973 (M^+). Calcd for $C_{17}H_{30}O_2Si$: *M*, 294.1996].

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